Combatting Rancidity due to Oxidation in Fish Oil Supplements with PharmaKeep®

Application Data

Oxidative Degradation in Fish Oil

Fish oil is rich in long-chain polyunsaturated fatty acids (PUFAs), particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). These fatty acids contain multiple double bonds, which make them highly susceptible to lipid peroxidation, a chain reaction that degrades the oil, leading to loss of nutritional value (EPA/DHA breakdown), off-flavors, unpleasant odors, and potentially harmful compounds.

A complex oxidation process occurs in PUFAs. Initially, heat, light or metal ions (often from blood due to physical damage to the fish) catalyze the abstraction of a hydrogen atom from a methylene group adjacent to a double bond in a PUFA. The lipid radical then reacts with molecular oxygen (O_2) to form a lipid peroxyl radical (LOO•), which can then abstract a hydrogen atom from another lipid molecule to form a lipid hydroperoxide (LOOH) and another lipid radical, and the chain reaction continues. Decomposition ensues as the unstable lipid hydroperoxides create secondary oxidation products, such as:

- **Aldehydes** (e.g., malondialdehyde, 4-hydroxynonenal)
- **Ketones**
- **Alcohols**
- **Short-chain hydrocarbons**

These compounds are responsible for the rancid odor and taste of oxidized fish oil and may have cytotoxic or genotoxic effects.[1]

Several factors can accelerate the rate of oxidation:

- **Degree of unsaturation**: DHA (22:6) is more prone to oxidation than EPA (20:5)
- **Presence of pro-oxidants**: Transition metals and UV light
- **Oxygen availability**: Even trace amounts can sustain the chain reaction
- **Temperature**: Higher temperatures increase reaction rates

The peroxide value (PV) is a critical indicator used to assess the oxidative stability and freshness of Omega-3 fish oil products. PV quantifies the concentration of lipid hydroperoxides, which are the primary products formed during the initial stages of lipid oxidation. Thus, low PV indicates a fresh product with minimal oxidation, while a high PV suggests that the oil has already begun to degrade and may soon develop off-flavors and odors.[2] The Global Organization for EPA and DHA Omega-3s (GOED) voluntary monograph recommends a maximum PV of 5 meq/kg for finished fish oil products, a colorimetric limit (p-Anisidine Value; pAV), and a calculated limit based on PV and pAV (TOTOX). The GOED limits are as follows.[3]

Parameter	Limit
Peroxide Value	5 meq/kg
p-Anisidine Value	20
TOTOX	26

A multi-year rancidity analysis from the Journal of Dietary Supplements revealed that 68% (23/34) of flavored and 13% (5/38) unflavored consumer Omega-3 supplements exceeded the TOTOX upper limits of ≤26, with 65% (22/34) flavored supplements and 32% (12/38) unflavored supplements failing the PV upper limit of ≤ 5, and 62% (21/34) flavored supplements exceeding the p-aV upper limit of ≤ 20.[4]

Whether oxidation of fish oils constitutes a significant health hazard continues to be studied among health scientists. Nevertheless, oxidation creates unhealthy free radicals and reactive aldehydes, fishy odors and off-flavors that negatively impact brand reputation, and food waste if products are not consumed prior to shelf-life expiry or rancidity.

Antioxidants

Antioxidants are key to maintaining oxidative stability of fish oils and maintain compliance with GOED limits. BHA, BHT, propyl gallate, TBHQ and ascorbyl palmitate are synthetic antioxidants commonly used in fish oil. There is also an increasing demand for 'clean label' solutions such as ascorbic acid, citric acid and its esters, and phenolic compounds (e.g. tocopherol, quercetin, rosemary extract and tea catechins).[5]

Packaging

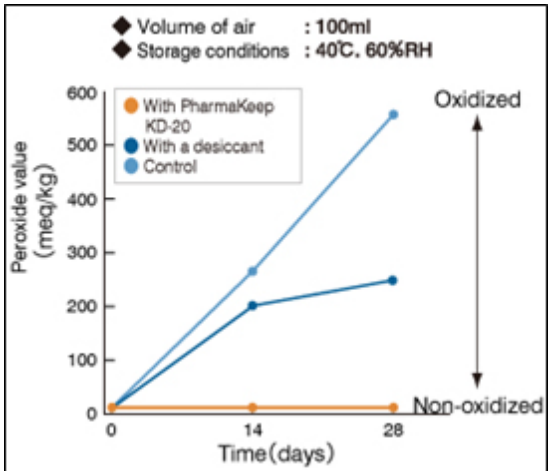
As established, oxidation is inevitable in Omega-3-rich oils. While antioxidants are added to slow this process, oxidation is reduced rather than prevented. Oxygen-protective packaging can be used to complement antioxidants or, in some cases, reduce the required antioxidant concentration.

PharmaKeep®

PharmaKeep® oxygen scavengers, available as drop-in canisters or packets, can be ideal for use with soft gelatin fish oil capsules. Because it is humidity neutral, PharmaKeep is specifically designed for pharmaceutical and nutraceutical applications - it does not require humidity in order to function. PharmaKeep readily absorbs the headspace oxygen that helps sustain the oxidative chain reaction. Unlike other oxygen scavengers, PharmaKeep is non-iron-based and will not introduce pro-oxidants to the packaging.

As indicated in the chart below, by using PharmaKeep in a sealed high barrier container, the PV of DHA is maintained at an extremely low level, effectively suppressing oxidation.

Prevention of degradation and oxidation for nutraceutical supplements containing DHA (47%) [6]



Furthermore, soft gel capsules generally have a 4-10% moisture content. Moisture content that exceeds 11% increases the risk of capsule adhesiveness and agglomeration. The PharmaKeep formulation contains a proportion of desiccant to help maintain an equilibrium relative humidity to support capsule integrity.

Barrier Bottles

PharmaKeep is compatible with most bottle systems with adequate structural integrity. The container-closure-system must be robust enough to endure the negative pressure created by the absorption of headspace oxygen. Many fish oil supplements are packaged in bottles made of polyethylene terephthalate (PET), which functions as a moderate oxygen barrier. Ideally PET bottles should be colored to block UV light, which as noted above is a pro-oxidant. For a higher level of barrier, OXYNOV® Barrier Bottles contain a layer of ethylene vinyl alcohol (EVOH) can provide a high level of barrier for the most sensitive formulations. Monolayer high-density polyethylene (HDPE) bottles have poor oxygen barrier properties and should be avoided for oxygen sensitive products.

Oxygen Transmission Rate (OTR) @ 73°F (23°C) / 0% RH cc/100 in²/24 hr [7]		
Material	**OTR**	**Barrier Performance**
HDPE	150-200	Poor
PET	2-6	Moderate
EVOH	0.005-0.12	Excellent

Conclusion

An optimal strategy for combating oxidative stress in fish oil capsules and maintaining their quality and shelf-life can involve a synergistic approach that includes:

- Incorporating antioxidants (potentially at lower concentrations)
- Utilizing oxygen scavengers (e.g., PharmaKeep)
- Employing adequate barrier packaging (e.g. OXYNOV)

References

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